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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/464,158	12/16/1999	ERLING SUNDREHAGEN	697.011US1	7192

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 12/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/464,158	SUNDREHAGEN	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *13-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendment filed September 9, 2003 has been entered. Claim 1 has been amended. Claims 13-17 have been withdrawn. Claims 18-23 have been newly added.

Election/Restrictions

2. Newly submitted claims 18-22 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The method for the assessment of elevated alcohol consumption is an unrelated method. This method has different steps, i.e., separating the carbohydrate free transferrin wherein at least 60% of the transferrin molecules in the carbohydrate-free transferrin containing fraction are carbohydrate-free transferrin molecules. The method of originally presented group does not produce the same results. Each group produces different effects and different functions when compared to the originally selected group. Therefore, the inventions are unrelated. These inventions are distinct and have acquired a separate status in the art because of their recognized divergent subject matter as exemplified by being classified in different classes and subclasses. Further, a search for the invention of the two groups would not be coextensive because a search indicating the process is novel or unobvious would not extend to a holding that the product itself is novel or unobvious; similarly a search indicating that the method is known or would have been obvious would not extend to a holding that the newly added process is known or would have been obvious. Because of the different steps based upon the use of different and

distinct compounds, a serious burden is imposed on the examiner to perform a complete search of the defined areas in both the patent and non-patent literature. Therefore, because of the reasons given above, the restriction set forth is proper and not to restrict would impose a serious burden on the examination of this application.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 18-22 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 1-12 and 23 are under consideration in this office action.

Response to Arguments

4. Applicant's arguments filed September 9, 2003 have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The rejection of claims 1-12 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is maintained. There is no [illegible] step in the method that teaches how the determination of the content of carbohydrate-free transferrin in said sample wherein said content of carbohydrate-free transferrin is used in the assessment of elevated alcohol consumption correlates to the assessment of elevated alcohol levels. The

claims recite that the content is used in the assessment, however the claims fail to recite the actual assessment of elevated alcohol consumption. Thus, telling one of skill in the art what components are used in the assessment is different from actually assessing elevated alcohol levels.

Therefore the rejection is maintained despite applicants' belief that the amendment has overcome the rejection. This amendment is not persuasive, since the claims are incomplete and amount to a gap between the steps.

6. The written description rejection of claims 3 and 5 under 35 U.S.C. 112, first paragraph is maintained for reasons already of record. The rejection was on the grounds that the written description is not commensurate in scope with the claims drawn to mixtures thereof because neither the claims nor the specification teach how to obtain mixtures thereof.

Applicants' assert that originally filed claims comprise the language "mixtures thereof" and that pages 9,10 and 12 provide a detailed discussion of carbohydrate-binding ligands. However, the issue is that a combination of ligands is different than mixtures thereof. There is no teaching of a portion of matter consisting of two or more components in varying proportions that retain their own properties, i.e., the definition of mixtures thereof as supplied by applicant. Therefore, despite applicants' arguments to the contrary, mixtures thereof are not supported by the specification. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process as is the case here. Applicants' specification continuously point out

combinations of ligands, however combinations of ligands do not meet the claimed limitation of mixtures. Thus one of skill in the art could not immediately envision the claimed mixture thereof.

See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); *In re Ruschig*, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967) The trouble is that there is no such disclosure, easy though it is to imagine it. (emphasis in original); *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1328, 56 USPQ2d 1481, 1487 (Fed. Cir. 2000) ("the specification does not clearly disclose to the skilled artisan that the inventors ... considered the ratio... to be part of their invention .... There is therefore no force to Purdue's argument that the written description requirement was satisfied because the disclosure revealed a broad invention from which the [later-filed] claims carved out a patentable portion". Similarly, it appears that the instant case sets forth combinations of ligands and asserts that this combination of ligands is equivalent to mixtures of ligands. However, there is no actual disclosure of the claimed mixtures of ligands.

There is no guidance as to what the mixtures are. There is no ~~teacher~~ teaching of what ligands can or cannot be used in the mixture being claimed. The specification does not include structural examples of mixtures thereof, but rather only teaches combinations. Thus, the resulting mixtures thereof could result in mixtures not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named ligands, the skilled artisan cannot envision the detailed structure of the mixtures thereof, thus conception is not achieved until reduction to practice has occurred. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Therefore, despite applicants' arguments to the contrary, mixtures thereof are not supported by the specification. Thus "mixtures thereof" fails to meet the written description provision of 35 USC 112, first paragraph and the rejection is maintained.

7. The rejection of claims 1-12 and 23 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons already of record. The rejection was on the grounds that the preamble was drawn to a method for the determination of carbohydrate-free transferrin in a body fluid for use in the assessment of elevated alcohol consumption, however there are no steps within the method that teach how to use the determination in the assessment of elevated alcohol consumption.

There is no step in the method that teaches how the determination of the content of carbohydrate-free transferrin in said sample wherein said content of carbohydrate-free transferrin is used in the assessment of elevated alcohol consumption correlates to

the assessment of elevated alcohol levels. The claims recite that the content is used in the assessment, however the claims fail to recite the actual assessment of elevated alcohol consumption. Therefore, telling one of skill in the art what components are used in the assessment is different than actually assessing elevated alcohol levels. The rejection is maintained despite applicants' belief that the amendment has overcome the rejection. This amendment is not persuasive, since the claims are indefinite for failing to particularly point out and distinctly claim the subject matter.

8. The rejection of claims 1-3, 6-8 and 10-12 under 35 U.S.C. 102(b) as being anticipated by Sundrehagen (WO 91/19983) is maintained for reasons of record. The rejection was on the grounds that Sundrehagen teaches assessing the concentration of a subset of analyte variants within a group of different analyte variants, test kits and reagents composition for use in such method.

Applicants' argue that Sundrehagen does not teach or suggest the specific measurement of carbohydrate free transferrin (CDT). However Examples 7 teaches the assessment of CDT in sera from patient; Example 8 teaches the assessment of CDT in sera from patients using disposable minicolumns. The results discriminate between heavy alcohol consumers and individuals not abusing alcohol. Examples 9 and 10 both teach tests for CDT in serum. The test also teach using a reference curve based upon reference samples containing known percentages of CDT to judge the percentage of CDT found in the tested samples. Thus, Sundrehagen teaches the specific measurement and assessment of CDT, contrary to applicants' argument.

Applicants' urge that Sundrehagen uses antibodies to transferrin and does not suggest the use of carbohydrate-binding ligands. However Sundrehagen teach using

proteinaceous binding partners that include moieties that bind to carbohydrate groups. This binding step occurs during the separation phase wherein binding moieties in chromatography and immunochromatography methods which use antibodies as taught by Sundrehagen. Also taught are the use particles and other solids that can use antibodies as binders. Sundrehagen taught the use of binding agents that bind to carbohydrate groups that aid in the separation phase. Therefore, Sundrehagen teach the method as claimed, contrary to applicants' arguments.

Applicants' argue that the instant method only encompasses binding transferrin molecules whereas Sundrehagen teaches methods that encompass transferrin and variants of transferrin therefore the rejection should be withdrawn. However, Sundrehagen's method includes the binding of transferrin, therefore it meets the claim limitations. The MPEP section 2123 teaches that patents are relevant as prior art for all they contain, "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). Thus Sundrehagen contains binding of transferrin and the binding of other variants does not take away from the teaching that transferrin is also bound. Therefore applicants arguments are not persuasive since a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir.1998). Therefore applicant's argument is not persuasive especially when considering

applicants argument that it is not necessary to use fractionation methods when the instant claims require similar and functionally equivalent techniques.

Claims 10-12 are drawn to a kit. Sundrehagen teach carbohydrate-binding ligands, a separation means and detection means. Therefore, Sundrehagen meets the limitations of the claims. Contrary to applicants' argument that the kit is distinguished over the prior art because of the separation step, Sundrehagen teaches the same structural means supplied by the instant kit that have the same function. Therefore, this argument is not persuasive and there are no distinguishing differences between the kit of the prior art and the kit of the instant claims.

9. The rejection of claims 4-5 under 35 U.S.C. 103(a) as being unpatentable over Sundrehagen (WO 91/19983) in view of Pekelharing et al., (Analytical Biochem) is maintained for reasons already of record. The rejection was on the grounds that it would have been obvious at the time of applicants invention to use a modified ELISA by replacing the immobilized antibody or enzyme linked antibody with a lectin or other carbohydrate binding protein of Pekelharing et al., (Analytical Biochem) in the method of assessment of alcohol consumption as taught by Sundrehagen, because Pekelharing et al., teach that the use of lectins increases the speed, specificity, sensitivity and simplicity of an immunoassay.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one having

ordinary skill in the art would have been motivated to make such a change such as a alternative and functionally equivalent modified ELISA since only the expected results would have been obtained. The prior art clearly teaches replacing the immobilized antibody or enzyme linked antibody with a lectin or other carbohydrate binding protein to create a heterologous lectin-enzyme immunoassay system.

Therefore, a skilled artisan would have had a reasonable expectation of success in switching the lectins. The use of an alternative technique would have been desirable to those of ordinary skill in the art based on the fact that the modified immunoassay has: 1) increased sensitivity when subfractions are to quantitated; increases the captured protein; 2) increased binding affinity; and 3) increased speed, specificity and simplicity when microtiter plates are used. Therefore the clear teaching of the prior art and the desirable techniques of the prior art would provide one of skill in the art with a reasonable expectation of success, contrary to applicants' argument.

In response to applicant's arguments against the Pekelharing reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Therefore it would have been prima facie obvious at the time of applicants' invention to use a modified ELISA by replacing the immobilized antibody with a lectin because Pekelharing et al., teach that the use of lectins in the place of antibodies increases the speed, specificity, sensitivity and simplicity of the assay. Therefore the rejection is maintained.

10. The rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Sundrehagen (WO 91/19983) in view of Dreher et al., Canadian Patent 2,074,345 is maintained for reasons already of record. The rejection was on the grounds that no more than routine skill would have been required to use well known methods for transferrin determination using immunoturbidimetry and immunonephelometry techniques as taught by Dreher et al., in the method of assessment of transferrin as taught by Sundrehagen, because Dreher et al., teach that immunoturbidimetry and immunonephelometry techniques can be easily and simply automated.

In response to applicant's assertion that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, it would have been prima facie obvious to modify the method of Sundrehagen (WO 91/19983) to incorporate determination using turbidometric or nephelometric means because Dreher et al., teach that immunoturbidimetry and immunonephelometry techniques can be easily used and simply automated. One would have a reasonable expectation of success since the techniques are based on interactions between antibodies and detected antigen, which Sundrehagen already teaches. Moreover, the turbidometric and nephelometric means have already been

used in the prior art to determine transferrin content. Therefore, one having ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent detection means since only the expected effects have been obtained. The prior art clearly teaches the detection of transferrin, therefore a skilled artisan would have had a reasonable expectation of success in exchanging the determination techniques. Moreover, the use of alternative and functionally equivalent determination techniques would have been desirable to those of ordinary skill in the based on ease and previous performance of said techniques.

Therefore, applicants' lack of motivation argument is not persuasive, and the rejection is maintained.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
November 23, 2004

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Application Number	Application No.	Applicant(s)	
	09/464,158	SUNDREHAGEN	
	Examiner	Art Unit	
	Ja-Na Hines	1645	